Allergy Abstracts

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Asthma and Hay Fever

The Use of Demerol in Patients With Bronchial Asthma. Herschfus, J. A., Salomon, A., and Segal, M. S.: Ann. Int. Med. **40**: 506, 1954.

The effect of Demerol on the respiratory mechanism of patients with chronic bronchial asthma was studied. During a remission, an intramuscular dose of 100 mg. Demerol protected against the bronchoconstrictive effects of intravenous histamine in all of six subjects and against intravenous methacholine in all of five subjects. Observations were made on various pulmonary functions during an acute attack of asthma, before and after the administration of 50 to 100 mg. Demerol. Following the administration of Demerol,

total minute ventilation dropped toward the normal range and hyperventilation was diminished without a rise in the arterial blood carbon dioxide content. The maximal breathing capacity and vital capacity were found to be improved in most patients. However, the alveolar gas exchange did not increase after administration of Demerol. Respiratory depression or respiratory acidosis did not occur.

Mild side reactions to the drug, consisting of dizziness, sleepiness, nausea, and vomiting, were noted in several patients.

Demerol, in therapeutic doses, was found to be a useful and safe drug in the treatment of an acute attack of asthma and in status asthmaticus, particularly when the usual methods of treatment had failed or where fastness to epinephrine or aminophylline had developed. The drug must not be given too often or in excessive dosage in chronic bronchial asthma and should be used very cautiously, if at all, in combination with barbiturates. J. S.

Prophylaxis of Summer Hay Fever and Asthma. A Controlled Trial Comparing Crude Grass Pollen Extracts With the Isolated Main Protein Component. Frankland, A. W., and Augustin, R.: Lancet **1**: 1055, 1954.

Two hundred patients with typical grass hay fever, with or without seasonal asthma, were studied in an attempt to evaluate the therapeutic effectiveness of various types of grass pollen extract. Only patients who had never received therapy and who had strictly seasonal symptoms were chosen for the study. A purified pollen protein was prepared by means of ultrafiltration through a collodion membrane. This purified material was then dissolved in buffered saline for use in treatment. The ultrafiltrate of pollaccine (crude extract of pollen) was found, by paper chromatography, to contain pigments, carbohydrates, amino acids, and peptides. This ultrafiltrate was inactive when employed for skin testing, but it was employed for treatment "because it could conceivably have contained some clinically important factor not revealed by skin tests." The subjects were divided into four groups. One group was given the standard pollaccine; a second group, a purified pollen protein; a third group, phenol saline solution; and the fourth group, the ultrafiltrate of pollaccine (inactive by skin test). Seventy-nine per cent of the patients treated with pollaccine or with purified pollen protein had good results, whereas only 33 per cent of the patients treated with the ultrafiltrate or with buffered saline were improved. Equally good results were obtained with the purified protein and the crude pollen extract. The relief of the rather large group treated by placebo injections was attributed to the light pollen season during the year the study was made. The fact that the ultrafiltrate gave no better results than the buffered saline tended to rule out its importance as an antigenic stimulant. R. W.

A Consideration of Improved Methods of Nebulization Therapy. Miller, W. F.: New England J. Med. **251**: 589, 1954.

The inspiratory method (IM) of nebulization is criticized because it provides a relatively rapid respiratory rate and small inspired volume in a large functional residual capacity, a situation which results in poor penetration and distribution of nebulized medication. The new expiratory-inspiratory-pause method (EIPM) provides for a pause at the end of a slow, natural, but not maximal, inspiration to permit improved distribution and deposition of nebulized particles. In this method, the patient is asked to exhale fully but not forcibly. Eight emphysematous patients, three with bronchial asthma, four

with chronic bronchitis, and one with bronchiectasis, were treated with nebulized bronchodilators by the inspiratory and by the expiratory-inspiratory-pause methods. The results of these two methods of therapy were compared in tests for pulmonary function. It was found that the EIPM invariably produced a greater increase in measured functions, particularly those likely to be affected by obstruction of airways; that is, the expiratory vital capacity, one-second vital capacity, and maximum breathing capacity. In both methods of therapy, the Vaponefrin nebulizer was combined with various types of masks and bottled gas under pressure. Several different types of nebulization apparatus and aerosol medications are evaluated. E. W.

An Open Circuit Helium Method for Measuring Functional Residual Capacity and Defective Intrapulmonary Gas Mixing. Hickam, J. B., Blair, E., and Frayser, R.: J. Clin. Invest. **33**: 1277, 1954.

An unequally ventilated lung presents a problem in measuring functional residual capacity because of the errors resulting from unequal mixing. To measure this factor, subjects were allowed to breathe a mixture of 50 per cent helium and 50 per cent oxygen for a fifteen-minute stabilization period. The subject was then given 100 per cent oxygen and the expired air was collected and analyzed for helium content. By using a katharometer system, continuous readings of the expired helium concentrations are possible in the range of 3 per cent to 0.05 per cent. Functional residual capacity of the lung can be calculated from the volume and helium concentration of the collected gas. Correction factors are presented in detail. When gas mixing in the lung is grossly uneven, the volume and ventilation rate of the slowly ventilated lung spaces may be estimated. Bottles were used as model lungs to prove the concept that "the excretion of an inert gas from lungs with uneven mixing proceeds as though the lung consists of a number of subdivisions each of which is ventilated homogeneously at its own rate." Blood absorption of helium was found to be too small to affect the respiratory curves significantly. Helium excretion curves were carried out on fifteen normal young men and on sixteen patients with pulmonary emphysema. The latter showed very large lung spaces with very slow ventilation rates. It was noted that the ventilation pattern changed strikingly in asthmatic patients following improvement and following treatment with bronchodilator drugs. The helium method does not describe the behavior of the rapidly ventilated lung spaces, but it does compare the ventilation rate of the slowly ventilated segments with total ventilation rate and functional residual capacity. The nitrogen method may grossly underestimate functional residual volume in patients with poor intrapulmonary mixing. K.

Role of the Friedländer Bacillus in Chronic Respiratory Disease. Fulton, J. K., and McKinlay, B. C.: Ann. Int. Med. **40**: 245, 1954.

The Friedländer bacillus usually has been considered to be an uncommon cause of disease. The type of pneumonia produced by infection with this organism is usually fulminating, with a tendency to lung cavitation. The mortality rate has been high. These infections are usually resistant to treatment with penicillin and the sulfonamides, but have responded to the newer broad spectrum antibiotics. Many mild cases of Friedländer pneumonia are thought to go unrecognized and may end as chronic Friedländer bronchitis, chronic lung abscess, or bronchiectasis.

Eight cases of pulmonary infection with Friedländer bacillus, diagnosed as chronic bronchitis, bronchiectasis, lung abscess, or asthma with bronchitis,

are described in detail. The presence of green putrefactive sputum and a poor response to penicillin should lead to a search for the Friedländer bacillus. A change in appearance of sputum from yellow to green while the patient is on antibiotic treatment should initiate a search for a previously overlooked Friedländer bacillus. The organism is morphologically similar to *B. coli* and probably is often overlooked as a sputum pathogen. A method for isolating the organism is described.

The three cases of asthma observed by the writers improved remarkably when the bronchial infection was cleared up with intensive antibiotic therapy.

J. S.

Dermatology

Effect of Dicumarol on Localized Shwartzman Reaction. Rothfeld, B., Williams, C. H., Thaler, W. J., and Rodas, J. M.: Proc. Soc. Exper. Biol. & Med. **87**: 5, 1954.

Rabbits were given daily doses of Dicumarol until their prothrombin times reached forty seconds. Each animal was then given a preparatory intracutaneous injection of meningococcus toxin, followed in twenty-four hours by a provocative intravenous injection of diluted toxin. The skin sites were then inspected. There was no significant difference in the production of dermal hemorrhagic necrosis between Dicumarol-treated animals and untreated controls. The effect of Dicumarol differed from that of heparin, which has been shown to exert an inhibiting influence on the dermal Shwartzman reaction.

M. C.

Cheilitis Due to Coffee. Lupton, E. S.: Arch. Dermat. & Syph. **68**: 333, 1953.

A 39-year-old housewife gave a history of dry, painful, scaly, and fissured lips for eight months. Her past history was negative for allergy. Patch tests with all her cosmetics, soaps, and dentifrices, as well as with those used by her husband, gave negative reactions. Because coffee was suspected as a possible cause for mild gastrointestinal symptoms, it was eliminated from her diet. Within ten days her lips were almost completely healed and her indigestion had ceased. The patient had not been in the habit of drinking unusually hot coffee and could tolerate hot tea without difficulty. A patch test with coffee of the same concentration which she drank gave a 2-plus reaction within forty-eight hours. On two separate occasions after being symptom-free for many months, the patient reproduced her symptoms by the ingestion of coffee.

R. W.

The Use of Cortisone During Penicillin Treatment of Secondary Mucocutaneous Syphilis in a Hypersensitive Patient. Brodey, M., and Nelson, C. T.: New England J. Med. **250**: 1069, 1954.

The use of cortisone during penicillin treatment of syphilis in a patient who was unusually hypersensitive to penicillin is reported. The patient, a 30-year-old man, reacted to small doses of the antibiotic with a severe serum sickness type of reaction or with bullous reactions in the skin. Cortisone controlled the urticaria and angioedema induced by penicillin during the course of antisyphilitic treatment. It was believed that the need for intensive treatment, as evidenced by mucocutaneous relapse and the persistence of positive spinal fluid findings, justified the use of cortisone to control the allergic manifestations which could not be controlled by antihistaminics.

E. W.

Eczematous Hypersensitivity to Coal Tar (Report of Three Cases). Simon, C. R., and Brandt, R.: Arch. Dermat. & Syph. **68**: 584, 1953.

Three patients who showed positive patch reactions to crude coal tar were studied. Only two of these individuals were available for patch testing with the various fractions procured from coal tar. In these two patients, completely negative reactions were obtained with the following fractions: benzene, xylene, toluene, phenol, pyridine, quinoline, anthracene powder, phenanthrene powder, and synthetic tar. Since shale oil is used for therapeutic purposes quite extensively and closely resembles coal tar, these patients were also patch tested with shale oil. Although weak solutions of the oil were employed, positive reactions were obtained. The ointment bases (neobase, zinc oxide, and petrolatum) all gave negative reactions. Each of the four fractions obtained from the shale oil was used for patch testing in a 100 per cent concentration. One patient showed a positive reaction to the cracked residuum, while the other patient had a positive response to the heavy distillate. Patch tests with the light distillate and with the uncracked residuum fractions yielded negative reactions in both patients. None of the shale oil fractions were found to be irritating when used for testing on control subjects.

This information seems to confirm the fact that mixed constituents do not result in a product identical with tar obtained before fractional distillation. It further substantiates the fact that crude coal tar is often more effective therapeutically than synthetic coal tar. R. W.

Dermatitis From Waterless Hand Cleaners. Morris, G. E.: Arch. Indust. Hyg. **9**: 507, 1954.

Waterless hand cleaners recently introduced into industrial use are basically aliphatic hydrocarbons which are primary irritants as well as sensitizers. Nine cases of vesicular dermatitis of the hands, resulting from the use of these cleaners containing aliphatic hydrocarbons of the naphtha series, are reported. F.

Histopathology of Allergic Dermatoses. Pinkus, H.: Ann. Allergy **12**: 671, 1954.

Allergic skin reactions are classified as being of the (1) epidermal, (2) urticarial, or (3) tuberculin type. These reactions are characterized by "no organic changes, no tissue alterations . . . which are in and of themselves pathognomonic for allergy." Nonallergic conditions mimic almost every reaction based on allergy.

The epidermal type of allergic response occurs in those dermatoses caused by external contactants and cannot be distinguished from those produced by primary irritants. The pathologic changes which occur in the eczematous contact type of dermatitis very likely begin in the epidermis, there liberating certain noxious substances which in turn provoke the vascular reaction seen in the corium. Epidermal edema leads to spongiosis and then to intraepidermal vesicle or bullae. Regeneration of new cells may begin while the acute phase is still in evidence. As the condition becomes chronic, lichenification and oozing commonly occur.

Among the urticarial type of reactions, the author places a large number of dermatoses, including chronic neurodermatitis, exudative neurodermatitis, atopic dermatitis, bullous urticaria, toxic erythema, allergic purpura, allergic granulomatosis, erythema exudativum multiforme, erythema multiforme bullosum, and periarteritis nodosa. These are grouped together because of their

morphologic similarity which lies in the fact that all are intimately connected with a vascular reaction which may result, in most cases, from a soluble antigen being brought to the skin by the blood stream. The acute urticarial wheal is characterized by a dilatation of capillaries, exudation of fluid through the vascular wall, and the accumulation of eosinophils in the perivascular tissue. It is from this point that the various dermatoses of this group take their respective characteristic forms.

In the tuberculin type of allergic response, the tissue changes are of the chronic granulomatous inflammatory type. In the human skin, the tissue responses may vary greatly, depending on the degree of immunity, the number and virulence of the invading organism, the route by which it reaches the skin, and the exact site at which it localizes. The important consideration, however, is that in the tuberculin type of reaction a relatively insoluble allergen is deposited in the substance of the skin and remains and acts there for a considerable length of time. This is in contradistinction to contact reactions where the antigen acts on the epidermis from the outside and to the urticarial reaction where soluble allergens are brought in contact with the skin by the blood stream. F.

Cutaneous Anergy and Hodgkin's Disease. Schier, W. W.: New England J. Med. **250**: 353, 1954.

The reactions to the intracutaneous injections of five antigens and of histamine were studied in thirty-three ambulant patients with Hodgkin's disease, in sixty-four controls, and in seventeen additional patients with other systemic disorders. The antigens consisted of: purified protein derivative (P.P.D.) of intermediate strength, histamine phosphate 1:1000 dilution, extracts of *Candida albicans* and *Trichophyton gypseum* in a dilution of 1:150, normal allantoic fluid of chick embryo, and mumps virus antigen. No significant difference was noted in the skin responsiveness to histamine in the patients with Hodgkin's disease and in the control group. To tests with mumps antigen, 86 per cent of the control group and 18 per cent of Hodgkin's group were positive. To *C. albicans,* 92 per cent of the control group and 21 per cent of the Hodgkin's group gave positive reactions. To *T. gypseum,* 72 per cent of the controls and 27 per cent of the patients with Hodgkin's disease were positive. To P.P.D., 72 per cent of the controls were positive, as compared to 21 per cent of the patients with Hodgkin's disease. Six patients with Hodgkin's disease had received cortisone; fifteen, nitrogen mustard; and twenty-four had been treated by irradiation. The possible significance of the modalities on the results of skin testing was minimized. One patient with Hodgkin's disease and another with myelogenous leukemia had noted pronounced amelioration of allergic rhinitis and asthma a year before the diagnosis of the principal diseases had been made. It was suggested that patients with Hodgkin's disease fail to produce antibodies in normal quantities. E. W.

Pruritus Produced by the Zooea Larvae of One of the Porcelain Crabs. Zinn, D. J.: J. Parasitol. **40**: 233, 1954.

Stinging and itching of the skin were noted by children while bathing in a small embayment near Cape Cod, Massachusetts. Symptoms persisted for about thirty minutes after drying and dressing. There were no visible lesions, but minute white translucent barbs were found at the site of stinging and were identified as the zooea larvae of a small porcelain crab. K.

Miscellaneous Allergies

A Study of Illness in a Group of Cleveland Families. VI. Control Studies of Reactions to Oxytetracycline Hydrochloride. Katz, S., Badger, G. F., Jordan, W. S., Rosenbaum, H. B., and Dingle, J. H.: New England J. Med. **251**: 508, 1954.

The side reactions from small daily doses of oxytetracycline hydrochloride (Terramycin) were studied in 101 adults and children. The drug was administered in doses of 250 mg. twice daily to children under 12 and in doses of 500 mg. twice daily to persons 12 years of age or over. A placebo was administered to eighty-six persons with a similar age distribution. Symptoms encountered were classified as follows: gastrointestinal, respiratory, nonspecific, and miscellaneous. While the drug was being administered, 71 per cent of the persons in the drug group and 26 per cent of those in the control group complained of one or more gastrointestinal symptoms. Twelve per cent of the drug group and 18 per cent of the placebo group developed respiratory symptoms. Nonspecific symptoms, which included fever, headache, dizziness, muscular aches, weakness, malaise, listlessness, fatigue, chilliness, feverishness, and diaphoresis occurred in 19 per cent of the patients treated with the drug and in 17 per cent of the control group. Miscellaneous symptoms, such as pain or burning on urination, vaginal itching and burning, hot flushing with perspiration, rash or skin eruptions, sore and burning eyes, puffy eyelids, difficulty in focusing, and cracked lips occurred in 12 per cent of the drug group and in 6 per cent of those treated with the placebo. Three patients in the drug group exhibited a fine morbilliform rash on the back or chest, while none of the controls showed similar lesions. Three of the control group and one of the drug group had a dry rash or eczema of the face. Isolated single miscellaneous symptoms included external otitis and conjunctivitis in the drug group and pimples behind the ears and roseola in the control group. The side reactions to oxytetracycline hydrochloride fell into three principal classifications, namely, primary irritative effects on the gastrointestinal tract, effects secondary to alteration of bacterial flora, and allergic effects. The chief irritative effects were anorexia, nausea, and vomiting. Alteration of bacterial flora was probably the cause of loose, frequent stools or diarrhea, rectal pain and itching, abdominal distress, abdominal cramps, gas and rumbling, cheilosis, glossitis, stomatitis, pharyngitis, pharyngeal ulceration, vaginal pruritus, and pain or burning on urination. The morbilliform rashes observed in the present series were probably examples of the allergic effect of this drug. It was concluded that allergic phenomena are infrequent and not severe. E. W.

Desensitization of the Penicillin-Sensitive Patient. Alexander, L. J.: Arch. Dermat. & Syph. **68**: 323, 1953.

Patients and nurses on the syphilitic wards who were allergic to penicillin were successfully desensitized. To date, eight persons have been treated. Four of these case histories are discussed in detail. All the patients had either an erythematous eczematoid type of rash or a contact dermatitis. They were desensitized by graduated doses of either aqueous penicillin (penicillin G) or a delayed absorption form of penicillin. Some patients were started on 50 units of penicillin G. The dose was rapidly increased at three-hour intervals, so that within one week 200,000 units per injection was tolerated without a reaction. Other patients received 30,000 units of a delayed absorption penicillin on the first day. On each succeeding day, the dose was increased by 30,000 units until 300,000 units per injection was given without any untoward

reaction. Patients with contact dermatitis from penicillin were completely desensitized by this technique, so that they could continue to expose themselves to penicillin without difficulty. Those with reactions to penicillin of the serum sickness type were treated much more cautiously, as their sensitivity is likely to be of a permanent type. R. W.

Allergic Reactions to Bee and Wasp Stings. Mueller, H. L., and Hill, L. W.: New England J. Med. **249**: 726, 1953.

Seven severe reactions to the stings of bees and wasps in children were observed. Of the seven patients, three were atopic and four were nonatopic. Five of the seven children developed shock reactions within a few minutes after they had been stung. The other two developed severe general reactions manifested by generalized urticaria and asthma. Skin testing by the intracutaneous method with mixtures of paper wasp and bee extracts or with the individual extracts elicited positive reactions in five of the seven patients. All seven of these children were put on hyposensitization therapy with these antigens. No further stings occurred in four of the seven treated patients. Of the three who subsequently were stung, one responded with a shock reaction and the other two were unaffected except for moderate local reactions. In children, a 1,000,000 dilution of the suspected antigen should be employed for intracutaneous testing. If the reaction is negative, treatment should be begun with 0.1 ml. of this dilution. Dosage should then be increased once or twice a week until the maximal dose is reached, which for some patients is 0.3 or 0.4 ml. of a 1-100 solution. The top dose should be maintained once a month for three years. When there is doubt as to which insect caused the reaction, it is suggested that a mixture of paper wasp and bee antigens be employed in hyposensitization. E. W.

Febrile Syndrome During Prolonged Hydralazine Treatment for Hypertension. Feder, I. A.: New England J. Med. **251**: 272, 1954.

A bizarre syndrome manifested by hyperpyrexia, generalized muscular pain, severe weakness, anorexia, tenderness of the muscles, pain and swelling of the lips and ankles, and severe headache was observed in a 40-year-old man with hypertension who had been treated with hydralazine (Apresoline) for one year. The patient's temperature fluctuated between 102 and 105 degrees for more than a month. Laboratory data were essentially negative except for a 1-plus to 3-plus albuminuria. X-ray examination of the chest indicated cardiac hypertrophy and an electrocardiogram revealed the classic pattern of advanced strain of the left ventricle. Both of these findings antedated the febrile episode. Since drug therapy failed to influence the course of this temperature, ACTH, 25 mg. in 500 ml. of 5 per cent glucose in water, was given intravenously by slow drip over a period of twelve hours. This produced dramatic relief of the complaints and physical findings within five days. The patient was then put on cortisone, which was gradually reduced and finally discontinued in about four weeks. It was suggested that this syndrome constituted polyarteritis and that this condition was cured by ACTH and cortisone. E. W.

Löffler's Syndrome Following Use of a Vaginal Cream. Klinghoffer, J. F.: Ann. Int. Med. **40**: 343, 1954.

A case of Löffler's syndrome which developed following the use of a vaginal cream containing sulfonamide is presented. There was a direct association between vaginal instillations of the cream and acute exacerbations of

symptoms. Skin tests with the constituents of the cream gave negative reactions, except for lactic acid which gave a positive reaction. The fact that generalized muscular pains, nausea, and vomiting accompanied each exacerbation of the disease would seem to indicate that the lungs were not the only site of reaction. Löffler's syndrome should be recognized as a systemic allergic disease in which the lungs are the site of most prominent reaction. J. S.

Severe Anaphylactic Reaction From Oral Penicillin. Eisenstader, D., and Hussar, A. E.: Am. Pract. & Digest Treat. **5**: 783, 1954.

A 22-year-old woman with a negative personal history but a positive family history ingested a tablet containing 800,000 units of crystalline penicillin. Within ten minutes, she experienced sudden onset of nausea and then rapidly developed abdominal cramps, pruritus, pain in the hands, cold perspiration, and urinary and fecal incontinence. Shortly thereafter, she collapsed and remained unconscious for about twenty minutes. The pulse was rapid and feeble, and the blood pressure was 70/40. Epinephrine 1:1000, administered intramuscularly, was effective within fifteen minutes. The patient had received intramuscular penicillin four years before and oral penicillin five months prior to the reported incident without untoward effects. F.

Anaphylaxis

Passive Anaphylaxis in the Dog. A Quantitative Study. Dulaney, A. D., Fedor, E. J., Barlow, G., and Gideon, M.: Proc. Soc. Exper. Biol. & Med. **87**: 146, 1954.

Healthy mongrel dogs were injected intravenously with rabbit antisera to bovine serum albumin. At intervals up to thirty-six hours later, the animals were challenged by the intravenous injection of antigen. A dose of 21 mg. antibody nitrogen sensitized all dogs, approximately one-half of which died in anaphylactic shock following challenge. No correlation was found between the latent period after sensitization and the shocking dose of antigen. When animals were sensitized with 10.5 to 16.8 mg. antibody nitrogen, milder anaphylactic reactions developed upon challenge with antigen. These experiments provide quantitative data on passive anaphylaxis in the dog. M. C.

The Effect of Histamine Upon the Local Fixation of Antibodies in the Skin of the Guinea Pig. Benacerraf, B., Biozzi, G., and Halpern, B. N.: J. Immunol. **73**: 318, 1954.

Guinea pigs were injected intravenously with rabbit antisera to hen ovalbumin. Immediately afterward, minute doses of histamine were injected intracutaneously into sites on the abdomen. After two hours, ovalbumin and Evans Blue dye were injected intravenously and the animals were sacrificed ten minutes later. The intensity and size of the blue spots were read on the inside of the skin sites as a measure of the cutaneous anaphylactic reaction. Similar experiments were done in which mild irritative substances were used instead of histamine.

Passive cutaneous anaphylactic reactions were elicited at the histamine-prepared sites two hours after intravenous challenge with the antigen. In contrast, a twenty-four-hour latent period was needed to elicit such reactions in control animals. The local treatment of skin sites with mild irritants produced results similar to those obtained with histamine. It was concluded that

histamine and other mild inflammatory substances were able to cause the local fixation of circulating antibody. The evidence seems to favor the concept that these agents produced this phenomenon by increasing capillary permeability. M. C.

Pharmacology, Physiology, and Pathology

Studies on the Transfer of Lymph Node Cells. III. Effects of Variation in the Interval Between the Injection of Antigen Into the Donor and Collection of Its Lymph Node Cells. Harris, S., and Harris, T. N.: J. Exper. Med. **100**: 269, 1954.

Killed dysentery bacilli were injected into the hind foot pads of rabbits. The popliteal lymph nodes were removed at intervals varying from ten minutes to twenty-one days. A cell suspension of the nodes was injected intravenously into the recipient rabbits to transfer the lymph node antibody to the blood serum of the recipient. Agglutination studies were then carried out on the recipient's blood serum. Controls included recipient animals irradiated to curtail their antibody responses to contaminating traces of antigen in the lymph cell suspension and normal recipient rabbits injected with cell suspensions heated to 37° C. for twenty-four hours (or 52° C. for twenty minutes) to decrease antibody content.

Lymph node cells removed three or four days after the injection of antigen gave rise to the appearance of agglutinating antibody one day after administration to the recipient. Heat-incubated cells injected in some animals resulted in the appearance of antibody in low titer on the fourth to sixth day, with a rise in titer at about the seventh to ninth day. Lymph node cells removed from the donor more than four days after antigen injection resulted in a lower titer of antibody. No antibody transfers were obtained with cells removed after the fourteenth day following antigen administration.

Regional lymph node cells removed two days after antigen injection gave rise to the appearance of antibody in the recipient, not on the first day, but on the second day after transfer. Heat-treated cells removed at the same time did not initiate the appearance of agglutinins until the third day after injection into the recipient. Lymph node cells removed one day after antigen injection did not elicit the appearance of antibody in the recipient until the third day. Heated cells from the same one-day node also elicited the appearance of antibody on the third day. When irradiated rabbits were used as recipients for the one-day node suspension, antibody appeared on the third day after receiving unheated cell suspension, but no measurable amount of agglutinins was found for the first ten days when heated cell suspension was used. Lymph node cells removed only ten minutes after antigen injection elicited antibody in the serum of the recipient irradiated rabbit four days later and heating this cell suspension prevented the appearance of antibody. It is suggested that the cells of the lymph node might contain a mechanism for synthesis of antibody or a precursor to antibody which could be transferred into the recipient animal and give rise to the appearance of antibodies in the recipient. The maturation time of agglutinins to dysentery bacilli appears to involve a minimum period of about three days between the time the antigen is injected into the donor and the time agglutinins appear in the recipient, regardless of the time spent by the lymph node cells in each of the animals. K.

Cytological and Pharmacological Observations on the Release of Histamine by Mast Cells. Fawcett, D. W.: J. Exper. Med. **100**: 217, 1954.

The intraperitoneal injection in rats of distilled water or a compound designated as 48/80 was found to cause release of granules from the mast cells of the mesentery. If a sufficient dose was employed, destruction of the mast cells resulted. Other cellular elements were not histologically altered. Some of the injected solution was removed from the peritoneal cavity from one-half to one hour after its introduction and was assayed for histamine content on guinea pig ileum suspended in atropinized Tyrode solution. Neoantergan counteracted the contractions. The histamine content of the removed fluid could be correlated with the degree of histologic destruction of the mast cells. At fifteen to twenty minutes, the concentration of histamine was greater in the fluid from animals injected with distilled water, but, in fluids removed thirty minutes after injection, the 48/80 group gave higher readings. Control injections of Tyrode solution produced only very slight histamine release. Mast cells were still absent from the mesentery of animals which had been injected with compound 48/80 or distilled water seven to ten days previously. When compound 48/80 or water was injected into these animals, no histamine was found in the withdrawn fluid. Photographs are included. K.

The Fate of Hydrocortisone -4-C^{14} in Man. Hellman, L., Bradlow, H. L., Adesman, J., Fukushima, D. K., Kulp, J. L., and Gallagher, T. F.: J. Clin. Invest. **33**: 1106, 1954.

Crystalline hydrocortisone -4-C^{14} was injected intravenously, over a period of exactly thirty minutes, into human subjects. Blood, urine, feces, and expired air determinations for C^{14} were carried out at intervals following the infusion. One of the subjects had had surgical removal of both ovaries and adrenals. She was studied both while she was receiving 100 mg. hydrocortisone daily and at a time when hormone had been withdrawn for forty-eight hours. Another subject was given 0.25 mg. hormone and at a later date received this same amount of labeled hormone together with 100 mg. of unlabeled "carrier" hormone. A third subject received 1 μc. hydrocortisone -4-C^{14} with 100 mg. carrier hormone and a fourth was treated with only the tracer quantity of hormone (0.25 mg.). In all these subjects, the urinary excretion pattern was essentially the same; namely, 56 per cent of the radioactive material was excreted at the end of six hours, 72 per cent in one day, and 80 per cent by the end of the third day. The peak of excretion occurred during the second hour after injection. The average half-life of the administered hydrocortisone was 3.6 hours in all subjects and was independent of the physiologic state of the patient, the size of the dose, or the presence of supplemental hormone. In four days, on a single subject so studied, 9 per cent of the administered hydrocortisone was excreted in the feces. A blood specimen taken fifteen minutes following the cessation of the infusion, in one instance, revealed that a maximum of 13 per cent of the circulating radioactivity was present as unaltered hydrocortisone. An average of 12 per cent of the radioactive hormone products excreted thirty minutes after completion of the infusion was present in free or unconjugated form. This value dropped to 3 per cent after six hours. Expired air, taken as a twenty-four-hour collection, contained .05 per cent of the radioactive material administered. It is concluded that widely differing quantities of hormone are handled by the same removal mechanisms and without regard to tissue requirements. The suggestion is made that the hormone is rapidly metabolized and retained in the blood in

an intermediate state of breakdown before it appears in the urine. Urinary removal does not follow the pattern of direct renal clearance of unaltered hormone, and it is suggested that the hormone is rapidly removed from the blood to tissues and extracellular fluids, from which site it is released in a different form and then excreted by the kidney. K.

The Natural History of Experimental Glomerulonephritis Produced by Foreign Protein. Hamilton, J. D., and Fremes, N. E.: Am. J. Path. **30**: 127, 1954.

Renal lesions, resembling human diffuse glomerulonephritis, have been produced in animals. There has not been general acceptance, however, of the similarity between the human and experimental diseases. The objective of these experiments was to follow the course of renal lesions produced in rabbits by injection of foreign protein and to compare these lesions with those in man.

Repeated injections of horse serum were made in unilateral nephrectomized rabbits. Groups of animals were sacrificed at intervals of one, two, four, eight, sixteen, and thirty-two weeks. Detailed descriptions of the pathologic findings in these animals are presented.

It was concluded that human glomerulonephritis and the experimental disease in rabbits are fundamentally similar and that the etiology is hypersensitivity of the anaphylactic type. J. S.

The Effect of Theophylline With Ethylenediamine (Aminophylline) on Cerebral Hemodynamics in the Presence of Cardiac Failure With and Without Cheyne-Stokes Respiration. Moyer, J. H., Miller, S. I., Tashnek, A. B., and Bowman, R.: J. Clin. Invest. **31**: 267, 1952.

Cerebral blood flow was studied by the nitrous oxide technique on patients with congestive heart failure, ranging in age from 38 to 70 years. Aminophylline, 0.5 Gm., was then injected intravenously over a five-minute period and cerebral blood flow determinations were repeated at once and after forty-five minutes. Aminophylline increased cerebrovascular resistance and lessened cerebral blood flow. This could not be accounted for by changes in blood CO_2 and was judged to be a direct effect of aminophylline on the cerebral vessels. There was some increase in arteriovenous oxygen differences, but these were not sufficient to compensate for the decreased blood flow. Cheyne-Stokes respiration in three of four patients was changed to normal rhythmic breathing following aminophylline. This was attributed to stimulation of the respiratory center. K.

Histamine Metabolism in Diseases of the Liver. Mitchell, R. G., Butt, H. R., and Code, C. F.: J. Clin. Invest. **33**: 1199, 1954.

Animal experimental studies indicate that the liver plays a part in removing or conjugating histamine from the blood stream. The blood and urinary histamine levels were studied in seventeen patients with obstructive jaundice. The mean concentration of histamine in the blood of twelve healthy adults was 0.04 μg. per milliliter and the range was 0.067 to 0.12 μg. per milliliter. In seven patients with cirrhosis of the liver, the mean concentration of histamine was 0.067 μg. per milliliter, with values ranging from 0.037

to 0.121 μg. per milliliter. However, two patients in terminal hepatic coma had very low histamine levels. Urinary histamine levels and values for conjugated histamine were in the normal range. Cortisone, administered in a dose of 50 mg. every six hours for three days to two patients, caused a decisive fall in blood histamine levels and a raise in free histamine urinary excretion. In jaundiced patients, histamine blood levels correlated roughly with the intensity of pruritus, although in one cortisone-treated patient the histamine blood level fell from 0.067 to 0.025 μg. per milliliter with no relief from itching. In this patient, methyl testosterone, 20 mg. per day, had no effect on blood or urinary histamine levels but afforded almost complete relief from the itching. K.

The Cerebral Hemodynamic Response to the Xanthine Compound, Parephyllin (Diethyl-Aminoethyl Theophylline Hydrochloride). Moyer, J. H., and Snyder, H. B.: Am. Heart J. **47**: 912, 1954.

A new xanthine compound known as Parephyllin (in France, Soluphylline) was studied. The advantage of this compound is that it is not as irritating as aminophylline when given orally or by intramuscular injection. Cerebral hemodynamic studies on seven subjects were carried out with measurement of cerebral oxygen consumption. Renal plasma flow and glomerular filtration rates were also studied before and after the administration of aminophylline and Parephyllin. Aminophylline is known to reduce cerebral blood flow. Parephyllin had very little effect on cerebral blood flow or on cerebrospinal fluid pressure, with two exceptions. However, dizziness and anxiety were common complaints. Both glomerular filtration rate and renal plasma flow were reduced temporarily by Parephyllin in contrast to the tendency of aminophylline to increase these values. Parephyllin exerts only a weak diuretic effect. The arterial oxygen levels increased in nearly all the patients. It is suggested that this drug be investigated as a bronchodilator. The drug is said to be useful in correcting Cheyne-Stokes respiration. K.

Risk of Thromboembolic Complications From Cortisone Therapy. Russek, H. I., Zohman, B. L., and Russek, A. S.: Am. Heart J. **47**: 653, 1954.

Eighty-six consecutive patients with vascular diseases were given cortisone daily, the doses starting at from 200 to 300 mg. and diminishing over a period of about three weeks. Thirty-four of the test subjects had hemiplegia; twelve had apoplectic strokes; twenty-seven had acute myocardial infarction and, of these, twenty-five had shoulder-hand syndrome. Six patients had angina pectoris and five had angina pectoris with coronary insufficiency complicated by bronchial asthma, sympathetic ophthalmia, exfoliative dermatitis, or histamine cephalalgia. Two patients with congestive heart failure were treated for a complicating acute bursitis. Thromboembolic complications did not occur during, or for several weeks after, cortisone administration. The angina patients' symptoms were not aggravated. Restriction of salt intake and the administration of 3 grams of potassium chloride daily were routine in all cases. None of the hypertensive patients developed an increase in blood pressure, and no special problems in control of edema developed in either of the patients in congestive failure. It is concluded that the danger of thromboembolism from cortisone administration is relatively slight. K.

The Use of Citrus Flavinoids in Respiratory Infections. Biskind, M. S., and Martin, W. C.: Am. J. Digest. Dis. **21**: 177, 1954.

A combination of equal parts of citrus flavinoids and ascorbic acid proved to be effective in the treatment of such respiratory tract infections as acute rhinitis, acute follicular tonsillitis, and influenza. Among a group of twenty-three patients, ranging in age from 7 to 70 years, this combination favorably influenced the course of infection in twenty-one cases. The most effective dosage was found to be 200 mg. three times a day. The flavinoids are known to restore impaired capillary permeability and fragility, and it is through this action that the favorable results noted in this series are believed to have been brought about. F.

Anaphylactoid Inflammatory Responses to Preparations of Duodenal Intrinsic Factors and Gastric Mucin. Jasmin, G., Selye, H., and Steelman, S. L.: Am. J. Digest. Dis. **21**: 245, 1954.

Intravenously administered preparations of duodenal intrinsic factor and of gastric mucin produced typical inflammatory anaphylactoid reactions in the rat. Adrenalectomy enhanced and prolonged this reaction. F.

Miscellaneous

ACTH and Cortisone in the Treatment of Ulcerative Colitis. An Evaluation of Their Prolonged Administration. Elliott, J. M., and Giansiracusa, J. E.: New England J. Med. **250**: 969, 1954.

An impressive symptomatic response to therapy with ACTH or cortisone was obtained in twelve of thirteen patients with ulcerative colitis. Some of the patients gave parallel objective manifestations of improvement in the ulcerative process, as indicated by sigmoidoscopy in eight cases and, to a lesser extent, by x-ray examination in three patients. In one case, the colitis went into clinical remission. The remaining twelve patients have required continuous hormonal treatment to maintain symptomatic suppression of what is apparently a continuing process. In most of these patients there was a recurrence of symptomatology when the dose of hormone was reduced or when it was discontinued. When treatment with these drugs was again instituted, subjective improvement and a cessation of symptoms immediately followed. It was concluded that ACTH and cortisone have a favorable effect on ulcerative colitis; however, it is not known that the general course of the disease is significantly altered by their use. E. W.

A Standardized Antigen and Agglutination Technic for Human Brucellosis. Report No. 3 of The National Research Council, Committee on Public Health Aspects of Brucellosis. Spink, W. W., McCullough, N. B., Hutchings, L. M., and Mingle, C. K.: Am. J. Clin. Path. **24**: 496, 1954.

The Committee on Public Health Aspects of Brucellosis found only one standardized antigen which has given consistent results for several years. It is recommended that the standard antigen utilized for Brucella agglutination testing in human beings be the tube antigen prepared from *Brucella abortus*, strain No. 1119, by the Bureau of Animal Industry of the Department of Agriculture. This will be produced commercially by one or more of the pharmaceutical companies. The technic for the use of this antigen is given in detail. K.

Absorption of Protective Antibodies From Serum of Rats Immune to the Nematode Nippostrongylus Muris. Thorson, R. E.: J. Parasitol. **40**: 300, 1954.

Rats repeatedly infected with *Nippostrongylus muris* developed immune serum. Precipitins in this serum were absorbed with saline which contained secretions and excretions of larvae. This was then mixed with living *N. muris* larvae and injected into rats. Fewer larvae developed in control rats injected with unabsorbed serum. When immune serum was absorbed with a saline extract of ground-up larvae, however, no such protective effect was demonstrable. It was concluded that antibodies formed to the larvae proper are not protective, whereas antibodies formed to secretions and excretions of the larvae are protective. The mechanism of protection may be by way of interfering with the parasites' enzyme systems and nutrition. K.

Fatal Shwartzman Reaction During Antibiotic Therapy. Nelson, L. M., and Braslow, E.: Arch. Dermat. & Syph. **68**: 328, 1953.

A 5-month-old girl with measles was given immune globulin, penicillin, and chloramphenicol. One week later she developed a temperature of 102 degrees and a rash over the diaper area, for which an injection of procaine penicillin was administered. Within twenty-four hours the patient suddenly became severely ill. The papulovesicular lesions over the diaper area became hemorrhagic and eventually gangrenous. On the day on which the rash first appeared, the blood count showed 3,500 white cells with 42 per cent granulocytes. On the three succeeding days the total white cell count was normal, but the differential showed only from 2 to 18 per cent granulocytes. Only *Proteus vulgaris* grew out on the culture of material from the ulcers and on the blood culture.

At post mortem, the lungs showed vascular engorgement, but no inflammatory reaction. In some of the pulmonary capillaries, basophilic granular plugs were seen which, by Giemsa's stain, were found to consist of leukocytes and platelets. A diagnosis of Shwartzman reaction was made on the basis of the clinical picture, pulmonary capillary plugs, leukopenia, and neutropenia. The authors could not rule out the possibility that sensitivity to chloramphenicol or to penicillin caused the leukopenia and the fatal reaction, but considered it more likely that the entire picture was produced by a bacteremia secondary to the local Proteus infection. R. W.

A Study of the Blood Groups in Habitual Abortion. McNeil, C., Warenski, L. C., Fullmer, C. D., and Trentelman, E. F.: Am. J. Clin. Path. **24**: 767, 1954.

In a study of 404 married couples, eighty-five of whom had a history of repeated abortions, blood group determinations were carried out, including ABO and Rh tests, serum cross match of father's cells and mother's serum, and an indirect Coombs' test. The possibility of anti-A or anti-B immune bodies in the mother was also investigated where indicated. The data are classified with reference to the blood groups of the parents and the percentage of aborters in each of these groups. The percentage of aborters varied from 11 to 15 per cent of theoretically compatible matings in which the father was of Group O. When the father was of Group A and the mother of A, B, or O, 24 to 26 per cent were aborters. It is suggested that the complexity of Group A cell antigens may account for the observation that so many A type

mothers with type A husbands experienced repeated abortions. The percentage of aborters rose to 45 per cent in a group of thirty-one couples, in which an O type mother was married to a B type husband. In a group of sixteen couples, in which the mother was of Group A and the father of Group B, four couples, or 25 per cent, had had two or more abortions. Anti-A or anti-B antibodies were not found in forty unmarried student nurses and contrasted with a high incidence of anti-A and anti-B antibody among the mothers studied. Data on this point are to be given subsequently. Blood group incompatibilities are suggested as an important factor in the pathogenesis of abortion. K.